Lysophosphatidic acid

Overview: Lysophosphatidic acid (LPA) receptors (nomenclature as agreed by NC-IUPHAR Subcommittee on Lysophospholipid Receptors; Chun *et al*., 2002) are activated by the endogenous lipid derivative LPA. Originally identified as members of the endothelial differentiation gene (*edg*) family along with sphingosine 1-phosphate receptors, the gene names have recently been updated to *LPAR1*, etc. to reflect the receptor function of these proteins. The identified receptors can account for most, although not all, LPA-induced phenomena in the literature, indicating that a majority of LPA-dependent phenomena are receptor-mediated. Radioligand binding has been conducted in heterologous expression systems using [^{3}H]-LPA (e.g. Fukushima *et al*., 1998). In native systems, analysis of binding data is complicated by metabolism and high levels of nonspecific binding, and therefore the relationship between recombinant and endogenously expressed receptors is unclear. Targeted deletion of LPA receptors has clarified signalling pathways and identified physiological and pathophysiological roles. LPA has also been described to be an agonist at PPARγ receptors (McIntyre *et al*., 2003), although the physiological significance of this observation remains unclear (Simon *et al*., 2005). A probable sixth LPA receptor, LPA_6, has been recently reported (Yanagida *et al*., 2009).

Nomenclature	LPA_1	LPA_2	LPA_3	LPA_4	LPA_5
Other names	VZG-1, Edg2, *lp* $_{A1}$	Edg4, *lp* $_{A2}$	Edg7, *lp* $_{A3}$	p2y9, gpr23	GPR92
Ensembl ID	ENSG00000119438	ENSG00000064547	ENSG00000171517	ENSG00000147149	ENSG00000184574
Principal transduction	$G_{i/o}$, $G_{q/11}$, $G_{12/13}$	$G_{i/o}$, $G_{q/11}$, $G_{12/13}$	$G_{i/o}$, $G_{q/11}$, G_s	$G_{i/o}$, $G_{q/11}$, G_s, $G_{12/13}$ (Lee *et al*., 2007)	G_q, $G_{12/13}$ (Kotarsky *et al*., 2006; Lee *et al*., 2006)
Selective agonists	–	FAP10, FAP12 (Virag *et al*., 2003)	OMPT (Hasegawa *et al*., 2003)	–	–
Selective antagonists	Ki16425 (Ohta *et al*., 2003)	–	DGPP 8:0 (Ohta *et al*., 2003)	–	–

FAP12, VPC12249 and VPC32179 have antagonist activity at LPA_1 and LPA_3 receptors (Okusa *et al*., 2003; Virag *et al*., 2003; Bagga *et al*., 2004). The selectivity of these antagonists is less than two orders of magnitude. None of the currently available chemical tools have validated specificity *in vivo*.

Abbreviations: DGPP 8:0, dioctanoylglycerol pyrophosphate; **FAP10**, decanol phosphate; **FAP12**, dodecanol phosphate; **Ki16425**, 3-(4-[4-{(1-[2-chlorophenyl]ethoxy)carbonylamino}-3-methyl-5-isoxazolyl]benzylsulfanyl)propanoic acid; **OMPT**, 1-oleoyl-2-*O*-methyl-rac-glycerophosphothionate; **VPC12249**, (*S*)-phosphoric acid mono-[3-(4-benzyloxy-phenyl)-2-octadec-9-enoylamino-propyl] ester; **VPC32179**, (*R*)-phosphoric acid mono-{2-octadec-9-enoylamino-3-[4-(pyridin-2-ylmethoxy)-phenyl]-propyl} ester

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